A CASE OF AMYOTROPHIC LATERAL SCLEROSIS PRESENTING BULBAR SYMPTOMS, WITH NECROPSY AND MICROSCOPICAL EXAMINATION.*

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The cases of amyotrophic lateral sclerosis studied clinically and pathologically have not been very numerous, and the report of every case increases our knowledge of the disease. Wolff[1], writing in 1894, stated that though amyotrophic lateral sclerosis had been known for about thirty-three years, he had been able to collect only ninety cases from the German, French, English and Russian literature, and only fifty-six with necropsy. Collins[2] succeeded in finding seventy-two cases with necropsy in 1896. We hope, therefore, that the following case may be of interest.

C. K.; a male; a native of Ireland; a laborer; married, aged fifty-three years, was admitted to the Nervous Wards of the Philadelphia Hospital, June 14, 1892. His family history was negative as regards nervous diseases. His personal history was unimportant up to the beginning of the present affection. He denied venereal disease and alcoholic excesses.

For five or six months before admission he had complained of pains in both legs from the knee down. He would grow very tired by night, and was soon obliged to use a cane in walking. Rest in bed would generally relieve him so that in the morning his legs would feel all right. On admission to the hospital the legs were somewhat spastic with exaggerated reflexes. Cutaneous sensibility was not changed. He walked with crutches and regularly left the hospital in the summer season for a period of two months. One year after admission his feet began to swell, and this œdema recurred from time to time. Later, eczema rubrum of both legs developed. In the summer of 1895 he was unable to leave the hospital as before, the weakness and rigidity of the legs now necessitating a wheel chair. About this time also it was noted that his speech was becoming indistinct, and it gradually assumed a bulbar character; but long before this he stated he had lost the power of whistling.

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* Read at the twenty-fourth annual meeting of the American Neurological Association, May, 1898.

[1] Wolff: Zeitschrift für klin. Med., xxv., p. 326.

[2] Collins: Amer. Jour. of the Med. Sciences, cxi., 1896, p. 690.

The arms also gradually became spastic; the exact time at which these symptoms made their appearance is not known. It appears, however, to be beyond question that the involvement of the arms was not only subsequent to that of the legs, but also subsequent by several years, as spasticity of the arms is not mentioned in the earlier notes.

All of his symptoms gradually became more pronounced until April, 1897, when he became bed-ridden, had occasional retention of urine and loss of control over the bowel, and developed bed-sores over the sacrum, heels and elbows. Subsequently his general condition again somewhat improved.

At the examination on November 11, 1897, the following notes were made: He is found seated in a wheel chair. His arms are semiflexed, the position of the limbs suggesting lateral sclerosis. Voluntary movements are much restricted and exceedingly slow, and only very slight flexion of the thighs or legs is possible, while the feet are in extreme extension. Marked resistance is also offered to passive movements, especially at the knees and ankles. The muscles feel firm, but some general wasting of the legs appears to have taken place. The knee-jerks are much increased.

The voluntary movements of the arms are also much restricted, but less so than those of the legs. The arms cannot be extended at the shoulders to the normal degree, but the amount of movement is considerable. Much less movement is possible at the elbow, and still less at the wrist and fingers, contracture being most marked in these situations. The fingers can be extended slowly and with difficulty. Considerable resistance is everywhere offered to passive movements. General wasting is noted in both arms, more marked in the forearms. Wasting is also noted in both hands; the thenar and hypothenar eminences are somewhat flattened. All of the symptoms are slightly more pronounced in the right arm than in the left. The tendon reactions are all increased.

The head can be moved voluntarily in all directions, but the movements are somewhat slower than normal and slightly irregular and jerky. The patient sits with the head slightly flexed, and does not move it unless requested to do so. However, the movements of the head are much freer on the whole than the movements of the arms and legs. No resistance is offered by the neck muscles to passive movements.

The face presents no asymmetry. The mouth is held slightly open. When he is asked to show the teeth, the mouth is drawn very slightly to the right. He is able to compress the lips fairly well. He cannot whistle; on making the attempt the lips deviate slightly to the right, while the opening formed between them is large and somewhat irregular. No tremor of the lips is observed, but there is unmistakable irregularity or ataxia of movement while making the effort. There is no dribbling of saliva. The muscles of expression appear to be normal. When he is asked to protrude the tongue, the whole mass is protruded sluggishly and it is launched forward with evident effort and toward the right side. Fibrillary twitchings are evident on both sides of the tongue. The tongue as a whole seems slightly atrophied; the right half being slightly smaller than the left. Swallowing is performed with difficulty, though there is no regurgitation through the nose. In eating solid food the patient assists the tongue by pushing the food between his teeth with his fingers.

The patient talks with a nasal intonation as though the soft palate were paretic. Only faint movements of the soft palate are seen during phonation. The speech is drawling and indistinct, and the consonants are imperfectly formed. The voice appears to be slightly hoarse and its pitch lower than normal. (The larynx, unfortunately, was not examined.) The pupils react normally to light and in accommodation. The movements of the globes are normal in all directions.

There is some atrophy of the muscles of the shoulder girdle, but it is not marked. No noticeable changes are observed in the trunk, save that the chest is somewhat barreled. There is retention of urine and incontinence of fæces.

No sensory losses can be detected. Touch, temperature and pain sense appear to be normal. The only subjective symptom is occasional pain in the knees.

The patient's mental condition appears to be fairly normal, save that he manifests a marked tendency to causeless laughter and that his memory is not as good as formerly. The general visceral examination is negative. A small bed-sore is found over the sacrum.

Subsequently the patient's general condition again became worse. Complete paralysis of the sphincters and great general prostration gradually made their appearance. December 30th he suffered greatly from abdominal pain and passed large quantities of bloody urine. His condition became gradually worse day by day until finally respiration became labored, circulation failed. He died January 7th, 1898.

Necropsy.—The body is that of a well nourished male. Dark coppery discoloration of both feet is noticed, extending midway up the legs. The toes are very strongly flexed and the sole of the foot is markedly arched. A condition of equinovarus exists. Lividity of surface is noted posteriorly. The hands and arms are extended.

Abdominal Cavity.—On opening the abdomen the general appearance is normal, but on close examination a fold of intestine is found bound to the top of the bladder by recent adhesions. On tearing these free a gangrenous perforation of the top of the bladder is noted. This opening was entirely walled off by two loops of the sigmoid flexure of the colon. A thick layer of lymph is upon the bowel where it was adherent.

Thoracic Cavity.—No plural adhesions are found and no effusion in either sac.

Heart.—Pericardium is normal, but the heart muscle presents evidences of slight myocarditis. A few patches of beginning atheroma are found in the aorta.

Lungs.—The lungs are crepitant throughout and slightly emphysematous. The arteries are sclerotic.

Spleen.—Spleen is normal.

Left Kidney.—The suprarenal body is normal. The capsule of the kidney strips easily. The perirenal fat is much injected. The surface of the kidney is stippled with small white spots, the size of a pin's head. These are barely perceptible to touch. They seem to be small miliary abscesses. On section, a quantity of foul-smelling fluid ran out. Two or three stones are found in the substance of the kidney. The largest is about the size and shape of a jackstone. The cortex is of good size and injected. The pelvis is distended and much inflamed.

Right Kidney.—The suprarenal body is normal. The kidney has a cyst the size of a walnut, and several smaller ones are seen on section. It is much like its fellow except that it does not seem to be so much diseased. The pelvis is not dilated and contains no stones. The capsule strips easily.

Ureters and Bladder.—The bladder is small, ribbed, thickened, and has a diphtheritic-looking membrane covering its inner surface. The edge of the rupture is ragged and easily torn.

Liver.—The liver is normal. The gall-bladder contains a small quantity of thin yellowish bile, and one small mulberry calculus. The duct does not seem to be patulous, or at least no bile can be forced through.

The brain and spinal cord presented no gross abnormalities and were reserved for microscopical examination.

Microscopical Examination.—In the lumbar and cervical regions the anterior roots are normal, or very slightly altered when stained by ammonium carmine or Weigert's hæmatoxylin method, although the cells of the anterior horns are few in number, especially in the inner and posterior groups. Most of these cells when stained by thionin according to v. Lenhossék's method have processes and contain chromophilic elements and centrally situated nuclei. Many of the cells are greatly atrophied. The cells contain also a large amount of pigmentary substance, and occasionally a mass of so-called pigment is all that remains of a former cell. Complete chromatolysis, either central or peripheral, is not found in most of the cells, though in some of the smallest cells the chromophilic

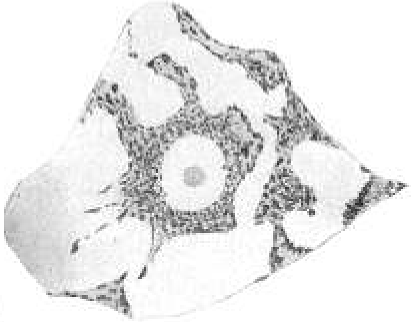

FIG. I. An anterior horn cell in which the chromophilic elements have undergone a peculiar form of degeneration.

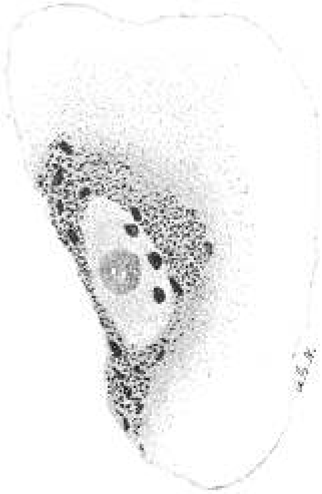

FIG. II. An anterior horn cell presenting a high degree of peripheral chromatolysis.

elements are broken into granules and no longer appear as elongated bodies. Occasionally transverse cleavage of the cell body may be seen. We have only been able to find one or two cells in which peripheral chromatolysis is very complete. In one cell we have noted the existence of what appears to be two nuclei. The atrophy of the cells of the anterior horns is much greater than that of the anterior spinal roots. The anterior horns throughout the cord, both by the carmine and Weigert's hæmatoxylin stain, are much less intensely colored than the posterior, and have a rarefied appearance. They contain comparatively few fibres. The posterior roots are normal.

The crossed and direct pyramidal tracts are much degenerated in the spinal cord, and yet they contain many normal fibres. The sclerosis involves a much larger portion of the anterolateral columns than the area occupied by the pyramidal fibres. The posterior columns in the lower cervical and upper thoracic region present a sclerosis which does not extend to the posterior commissure, posterior horns, or periphery of these columns. This sclerosis is not confined to any system of fibres and is only of moderate degree. The Marchi method reveals no recent degeneration. The degeneration of the pyramidal fibres is very distinct at the motor decussation, but above this becomes gradually indistinct, though the anterior pyra-

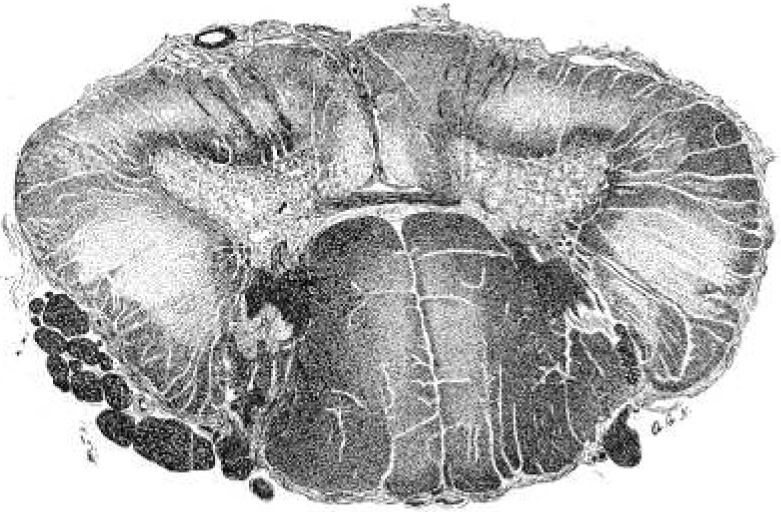

FIG. III. A section from the lower cervical region. The anterolateral columns, especially the pyramidal tracts, are much degenerated. The posterior columns are slightly degenerated. The anterior horns are less intensely stained than the posterior.

mids are very evidently diseased. The cells of Clarke's columns are apparently normal.

A portion of the external popliteal nerve was "teased" and placed in the fresh state in osmic acid. The fibres present some swelling of the myelin sheaths, but otherwise they are normal.

The facial and hypoglossal centres and the nucleus ambiguus are normal, though some of the cells are highly pigmented. The posterior nucleus of the vagus contains many cells showing great pigmentary degeneration, and masses of so-called pigment in some places are the only remains of nerve cells. Intramedullary portions of the vagus and hypoglossus nerves are apparently normal. The posterior longitudinal bundles are normal.

Round bodies are found immediately under the fourth ventricle at the level of the vagus and hypoglossus centres, and they are also found within the spinal cord. They are round, of various sizes, and when freshly stained seem to be surrounded by a clear space, but after the section has been kept for a time these bodies present a pale blue peripheral circle. These formations are the same whether the tissue is cut transversely or longitudinally. They stain a deep blue with thionin and retain the color very well, and are also colored by Delafield's hæmatoxylin. They are doubtless amyloid bodies.

Groups of round bodies are found in the medulla oblongata, especially about the vessels. They stain deep purple with thionin, but fade very soon to pink, and gradually lose all color. They may possibly be the colloid bodies of Bevan Lewis, and have been described by us[3] elsewhere. They do not seem to be the same as the amyloid bodies. When thionin is used and Lugol's solution applied afterward, the nerve cells, neuroglia cells and so-called colloid bodies stain a light mahogany color. The amyloid bodies have the same deep mahogany color as when the Lugol's solution is used alone.

Portions of one biceps muscle of the thigh appear to be normal. We were not able to remove any tissue from distal portions of the extremities. The tongue studied by the Marchi stain and by carmine is normal, and even its intramuscular nerve fibres are not diseased. Interstitial myositis is found in sections taken from one crico-arytænoideus posticus muscle of the larynx. The connective tissue here is hyperplastic and the nuclei are excessive. In some places areas of degenerated muscular fibres are found.

The giant cells of the paracentral lobule are not destroyed, but are not abundant. Numerous pieces of tissue were taken from different parts of each lobule, but only a few giant cells were observed. With this exception, the cortex seems to be normal.

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[3] Spiller: New York Medical Journal, Aug. 13th, 1898.

Portions of one paracentral lobule, hardened in formalin and stained by Marchi's method, reveal no traces of degeneration. Sections from the inner capsule, hardened in Müller's fluid and stained by the same method, give negative findings. Sections from the pons, cerebral peduncles and inner capsule reveal no degeneration by Weigert's method.

The columns of Goll are not infrequently affected when the pyramidal tracts are diseased, especially if the latter are primarily affected, and the colums of Goll in such cases stain more deeply with the carmine. This was the condition in a case of arrested development reported by one of us (Spiller[4]). According to Brissaud the columns of Goll are the most liable of all the spinal columns to degenerate.

Dejerine and Sottas[5] describe a case in which they found sclerosis of the crossed pyramidal tracts, not extending upward above the superior part of the cord. No appreciable change could be detected in the cells of the anterior horns, or in the anterior roots, and no muscular atrophy had been seen. In this case the columns of Goll were slightly sclerosed in the cervical and upper thoracic regions. Sensation had been normal during life. This case might possibly be regarded as one of amyotrophic lateral sclerosis in its early stages, beginning in the pyramidal tracts, and in this sense it would support the view of Charcot regarding the portion of the nervous system primarily affected in this disease. We are not warranted, however, in assuming that the peripheral neurons would necessarily have become involved.

Moeli[6] observed degeneration of the posterior columns in the lower cervical and upper thoracic regions in a case of amyotrophic lateral sclerosis.

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[4] Spiller: Journal of Nervous and Mental Disease, Feb., 1898, p. 87.

[5] Dejerine and Sottas: Arch. de Physiologie, July, 1896.

[6] Moeli: Archiv. für Psychiatrie, x., p. 718.

Marie[7] says that the columns of Goll in amyotrophic lateral sclerosis stain more deeply with the carmine than they do in normal spinal cords. He attributes this to alteration of the myelin sheaths, and probably to overgrowth of the neuroglia, which may be the result of lesions of the cells of the posterior columns situated in the spinal cinerea. Inasmuch as Lenhossék[8] finds that few cells of the cord send their axis cylinders into the posterior columns, we must be in doubt as to the correctness of this explanation.

Not infrequently the columns of Goll present a slight sclerosis in cases in which no sensory symptoms have been present, and there seems to be a relation in some way between this sclerosis of the columns of Goll and that of the motor system. Oppenheim[9], and Charcot and Marie[10] noticed sclerosis of the posterior columns of the cord in amyotrophic lateral sclerosis. Other cases are reported in which symptoms indicating involvement of the posterior columns were added to those indicating disease of long duration of the lateral columns. Brissaud[11] reports such a case. At the necropsy the lesions of amyotrophic lateral sclerosis and of incipient tabes were observed.

Degeneration of the posterior columns has been found in chronic anterior poliomyelitis. Nonne[12], in reporting a case of this disease, says he noticed a distinct, though not excessive, rarefaction of fibres in the median portion of the posterior columns. This was most evident in the cervical region, and was not limited to any system of fibres. The cells of the anterior horns were intensely degenerated. Inasmuch as primary degeneration of the pyramidal tracts was not observed, it seems reasonable to ascribe this degeneration of the posterior columns to the destruction of the cells in the spinal cinerea, and not to a primary degeneration of the nerve fibres. Experiments performed on animals in temporary closure of the abdominal aorta have given support to Marie's view and have shown that many cells within the spinal cinerea send their axis cylinders into the posterior columns.

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[7] Marie: Traité de Médecine, vi., p. 347.

[8] Lenhossék: Der feinere Bau des Nervensystems, etc.

[9] Oppenheim: Archiv. für Psychiatrie, xxiv., p. 758.

[10] Charcot and Marie: Archives de Neurologie, x., 1885, pp. 1 and 168.

[11] Brissaud: Leçons sur les Maladies Nerveuses, p. 34.

[12] Nonne: Berliner klin., Wochenschrift, 1896, p. 207.

Hektoen[13] described a case of amyotrophic lateral sclerosis in which sensory symptoms were noted later in the disease. He ascribed these symptoms to the lesions of the spinal ganglia, posterior nerve roots, columns of Goll, and the sensory portion of the fifth nerve. He regarded his case as a sort of connecting link between progressive spinal muscular atrophy and amyotrophic lateral sclerosis on the one hand, and tabes dorsalis on the other.

A sufficient number of cases of combined systemic disease have been reported to show us that tabetic symptoms may appear at the same time as, or later than, those indicating disease of the lateral columns, but in cases of amyotrophic lateral sclerosis in which symptoms pointing to an affection of the posterior columns have not existed, the sclerosis of the columns of Goll is not always tabetic in its location within these columns, i. e., it is not systemic in character and is unlike that which we find with disease of the posterior roots. In our case the posterior roots are not degenerated, and the more deeply stained portion of the columns of Goll, by the carmine stain, is found in the lower cervical and upper thoracic regions, and does not extend to the posterior commissure or to the periphery of the cord. It is, therefore, very different from that which results from disease of the posterior roots, and appears to be a primary degeneration.

There is no reason why a person with amyotrophic lateral sclerosis should not acquire tabes, but what is the meaning of an apparently primary degeneration of Goll's columns such as has been noted in the case of spastic paralysis reported by Dejerine and Sottas (l. c.) or in our case and other cases of amyotrophic lateral sclerosis? In our case no symptoms indicated the existence of this slight sclerosis in the columns of Goll.

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[13] Hektoen: Jour. of Nervous and Mental Disease, 1895, p. 145.

The description of the pathological condition in amyotrophic lateral sclerosis as held by Charcot has not been accepted by all. Chief among the opposers Leyden may be mentioned. He has refused to accept amyotrophic lateral sclerosis as a sharply defined disease and believes it cannot be separated from progressive bulbar paralysis. He does not regard the spasticity as of great importance. Gowers also has not accepted Charcot's views. The case reported by Senator[14], and later by Wolff[15], does not favor Charcot's idea that the pyramidal tracts are affected in advance of the motor cells of the cord. This case is well known, and we need not refer to it in detail. The symptoms of amyotrophic lateral sclerosis were present in a person in whom the spinal motor cells of the cervical and thoracic regions were atrophied, and the pyramidal tracts were not degenerated. However, foci of softening were found in the cord, and the brain was not examined. The muscular atrophy is easily explained by the condition of the motor spinal cells. May we not venture to suggest that the foci of softening had some connection with the spasticity? Senator would have us use the name of bulbo-spinal spastic atrophic paralysis instead of amyotrophic lateral sclerosis.

We know that spasticity may be produced by cerebral lesions without sclerosis of the pyramidal tracts. We, ourselves, have seen cases in which the lesions occurred in early childhood and sclerosis of the motor tracts did not develop. Long ago Schulz[16] reported two cases without alteration of the spinal cord presenting the appearance of spastic spinal paralysis (lateral sclerosis). In one a cerebral tumor was found, in the other chronic internal hydrocephalus.

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[14] Senator: Deutsche med., Wochenschrift, vol. xx., 1894, p. 433.
[15] Wolff: Zeitschrift für klin., Med., xxv., p. 326.
[16] Schulz: Deutsches Archiv., für klin., Med., 23, p. 343.

We can easily understand, therefore, that while degeneration of the central and peripheral motor tracts has been found in most cases of amyotrophic lateral sclerosis, lesions of the peripheral motor neurons with some destruction of tissue in the brain or upper part of the cord, affecting the motor tracts indirectly, might also produce the clinical picture of amyotrophic lateral sclerosis, and yet the lateral columns be apparently intact.

The fact that the bulbar nuclei were, for the most part, normal in our case, while the degeneration of the motor fibres extended above these nuclei, seems to support Charcot's view in regard to the primary nature of the degeneration in the motor tracts, for it is in this way we would explain the symptoms of bulbar paralysis.

The case reported by Strümpell[17] would seem to justify Charcot's view, for certain instances at least. The pyramidal tracts were degenerated from the cerebrum to the lower lumbar region, and the cells of the hypoglossal nuclei and those of the anterior horns of the cord were not normal. The changes were much greater in the pyramidal tracts than in the cells, and Strümpell himself believed that the lesions originated in the central motor neurons.

Raymond[18] acknowledges that in the majority of cases amyotrophic lateral sclerosis cannot be separated from the labio-glosso-laryngeal paralysis, but he believes that in some cases the atrophy of the spinal motor cells or of the bulbar nuclei may be without involvement of the pyramidal tracts. He published in collaboration with Mathias Duval[19] a case in which the bulbar nuclei were affected and no trace of sclerosis of the motor tracts was seen. Raymond refers to a number of other cases of pure labio-glosso-laryngeal paralysis,—pure in the sense of being without involvement of the motor tracts.

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[17] Strümpell: Deutsche Zeitschrift für Nervenheilkunde, vol. v., p. 225.

[18] Raymond: Leçons sur les Maladies du Système Nerveux, Première Série.

[19] Duval and Raymond: Archives de Physiologie, 1879.

The arrest of the degeneration in our case in the bulbopontine regions follows the usual rule, though in some instances the degeneration has been traced higher, even to the cortex (Kojewnikoff[20], Charcot and Marie[21], Lemmelin[22], Lumbroso[23], Nonne[24], and Mott[25]).

Charcot and Marie reported two cases in which they found great diminution of the large pyramidal cells normally present in the paracentral lobule. The other cells of the cortex appeared to be normal. We take it that they refer to the giant cells of Betz. These are present in our case, but possibly are not as numerous as usual.

Marie[26] called especial attention to the fact that the degeneration of the lateral columns in amyotrophic lateral sclerosis involves a greater area than that occupied by the pyramidal tracts, as marked out by secondary degeneration from cerebral lesions, or by the myelination of the white columns. This degeneration in the lateral columns, extending ventrally beyond the crossed pyramidal tracts in an area called the supplementary zone (Marie, Brissaud), was supposed by Marie to be the result of degeneration of column cells in the spinal cinerea. Brissaud (l. c.) eagerly accepted this teaching and added to it. According to him, the pyramidal fibres in amyotrophic lateral sclerosis are not affected primarily, and even when the process has lasted some years, normal fibres may be found in the sclerotic areas. He believes that the malady involves primarily only short fibres, and that the pyramidal fibres may be affected secondarily. The short neurons throughout the cerebro-spinal axis are supposed to be diseased. This view does not seem to have gained many adherents.

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[20] Kojewnikoff: Archives de Neurologie, vol. vi., 1883, p. 356.

[21] Charcot and Marie: Archives de Neurologie, x., 1885, pp. 1 and 168.

[22] Lemmelin: Upsala lakaref, 1887, xxii., No. 7, p. 299, cited by Raymond.

[23] Lumbroso: Cited by Joffroy and Achard.

[24] Nonne: Neurologisches Centralblatt, 1894, p. 393.

[25] Mott: Brain, vol. xviii., p. 21.

[26] Marie: Bulletins et Mémoires de la Société Médicale des Hopitaux de Paris, 1893, p. 757.

J. B. Charcot[27] speaks especially of the degeneration of this supplementary zone in progressive spinal muscular atrophy and in this disease the pyramidal tracts are not affected. The fact that the pyramidal tracts are not degenerated shows that something more than degeneration of tract cells with their axis cylinders must occur in amyotrophic lateral sclerosis. The degeneration of the supplementary zone does not seem to be present in every case of progressive spinal muscular atrophy. In one of Dejerine's[28] two cases it was not detected and in the other it was so slight that its existence was questionable.

It is hardly fair to Oppenheim[29] to ignore the statement made by him in 1892 that the degeneration of this supplementary zone is due partially to atrophy of short fibres which degenerate secondarily to disease of the anterior horns. This supplementary zone is largest in the cervical and thoracic regions (Marie).

The tongue in our case does not show atrophy when examined microscopically. We have employed the method of Marchi in the hope of finding accumulations of fat drops within the muscular fibres, such as Obersteiner[30] has described in the tongue from a case of tabes, but we have not been successful. Joffroy and Achard[31] succeeded in finding atrophy of the lingual muscles in a case of amyotrophic lateral sclerosis, and the atrophy seemed to be more marked near the tip of the tongue.

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[27] J. B. Charcot, Thèse de Paris, 1895, Review in Revue Neurologique, 1895, p. 502.

[28] Dejerine: Comptes rendus de la Société de Biologie, 1895, p. 188.

[29] Oppenheim: Arch. für Psychiatrie, xxiv., p. 758.

[30] Obersteiner: Arbeiten aus dem Institut für Anatomie und Physiologie. etc., iii.

[31] Joffroy and Achard: Archives de Médecine Expérimentale et d'Anatomie Pathologique, 1890, vol. 2, p. 441.

Kronthal[32] also has found the lingual muscles degenerated in amyotrophic lateral sclerosis.

The posterior longitudinal bundle has been found degenerated in a number of cases of amyotrophic lateral sclerosis (Muratoff[33], Hoche[34], Mott (l. c.), and it is believed that the fibres of this bundle unite the nuclei of the motor cranial nerves. Muratoff (l. c.) found this bundle abnormal in three cases in which the nuclei of the motor cranial nerves were altered and normal in a fourth case in which these nuclei were not affected. This posterior longitudinal bundle is analogous to the anterolateral ground bundle of the cord, and Muratoff believes that he was the first to find the former degenerated in amyotrophic lateral sclerosis. Muratoff, writing in 1891, states that the anterolateral ground bundle had been found degenerated in amyotrophic lateral sclerosis by Moeli (poliomyelitis), Flechsig, Leyden, Vierordt, Gombault, Charcot and Marie, Roth, Strümpell and himself. Since this date many other observers have remarked upon this degeneration.

Oppenheim mentions especially that he found the posterior longitudinal bundle normal, contrary to the findings of Muratoff.

In our case this bundle of fibres is not degenerated, and its integrity is probably due to the fact that most of the motor cranial nuclei are apparently normal.

The hypoglossus nucleus and nucleus ambiguus in our case do not seem to be much affected, and the intrabulbar portions of the nerves arising in these nuclei are not degenerated. The cells of the posterior nucleus of the vagus are greatly degenerated and many of them consist almost entirely of so-called pigment. This may at first thought cause some surprise, for the nucleus is supposed to be sensory. Degeneration of these cells has been observed in a number of cases of amyotrophic lateral sclerosis. Muratoff in three cases of this disease, found atrophy of the hypoglossus nucleus, complete atrophy of the roots of the twelfth nerve in two cases and partial atrophy in a third. In all three cases the posterior nucleus of the tenth nerve was affected, but less so than the twelfth nucleus, and the nucleus ambiguus was perfectly normal. Oppenheim[35] speaks of the difficulty in judging of the condition of the anterior nucleus of the vagus, as its cells do not always form a compact group. In speaking of amyotrophic lateral sclerosis he says that Eisenlohr found the posterior nucleus of the vagus diseased in its

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[32] Kronthal: Neurologisches Centralblatt, 1891, p. 133.

[33] Muratoff: Neurologisches Centralblatt, 1891, p.512.

[34] Hoche: Neurologisches Centralblatt, 1897, p. 242.

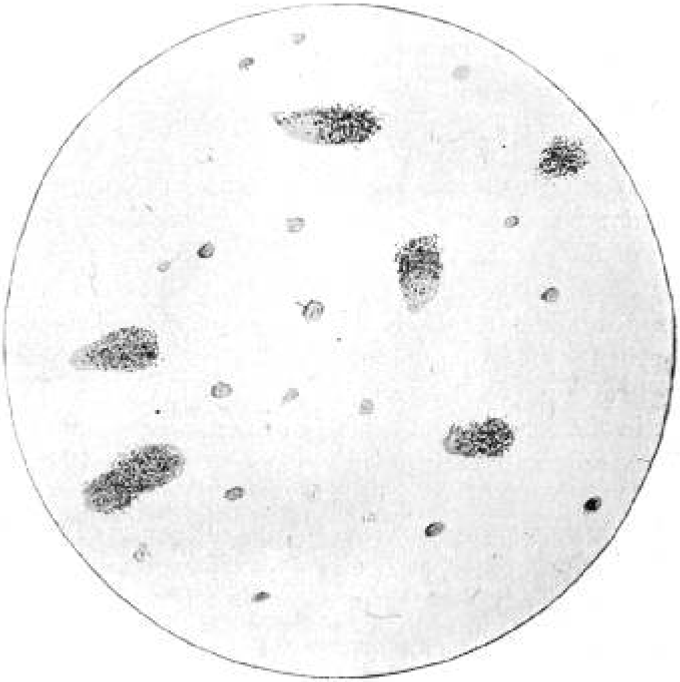

FIG. IV. Pigmentary degeneration of the posterior nucleus of the vagus.

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[35] Oppenheim: Archiv. für Psychiatrie, xxiv., p. 758.

lowest portion. Dejerine also found this posterior nucleus altered, while the anterior was normal, and Freund made a similar observation. Kronthal and he (Oppenheim) each found the posterior nucleus degenerated.

Marinesco[36] observed degeneration of the posterior vagus nucleus and concluded that this nucleus must be motor. Van Gehuchten[37], however, has offered a different explanation for Marinesco's findings.[38]

We mention, without attempting to draw any conclusions, that degeneration was found, not only in the posterior nucleus of the vagus, but also in one of the laryngeal muscles examined.

The anterior spinal roots in our case are only slightly degenerated. This is scarcely what we should expect in view of the extensive atrophy of the cells of the anterior horns, but it is well to remember that the condition of these roots is not entirely dependent on that of the cells. Senator[39] states that in his case with the symptoms of amyotrophic lateral sclerosis, the anterior spinal roots, even in the cervical and thoracic regions where the motor cells were greatly atrophied, were not notably degenerated.

While the nerves arising in the degenerated cranial nuclei in Kronthal's case of amyotrophic lateral sclerosis were also degenerated, the nerves arising in the cord were normal, although the cells of the anterior horns were entirely degenerated and the anterior roots were much altered. Kronthal states that the peripheral nerves have not often been studied in amyotrophic lateral sclerosis. As the peripheral ramifications of otherwise normal nerves in some cases of amyotrophic lateral sclerosis were diseased, Kronthal is inclined to believe that the degeneration of muscular tissue affects the nerve terminations. The case of muscular dystrophy studied by one of us (Spiller[40]) demonstrates the fact that the muscles may degenerate completely and the intramuscular nerve bundles still appear perfectly normal. Kronthal[41] is positive that degeneration of the peripheral nerves does not necessarily follow degeneration of the cells of the anterior horns of the cord. This cannot be said of the cranial nerves according to his views.

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[36] Marinesco: Comptes rendus de la Société de Biologie, 1897.

[37] Van Gehuchten: Centralblatt für Nervenheilkunde und Psychiatrie, Beiheft, Oct., 1897, p. 15.

[38] Considerable evidence has been offered by Mahaim in regard to the motor functions of the posterior nucleus of the vagus. Journal de Neurologie, No. 13, 1898, p. 259.

[39] Senator: Deutsche med. Wochenschrift, vol. 20, p. 433.

Oppenheim[42] makes very clear statements in regard to this question. According to him, even when the anterior cells of the cord are almost entirely destroyed, the anterior roots may not be notably altered, and when the anterior cells are normal, or nearly normal, a moderate atrophy of the anterior roots may be found. The explanation for this he is unable to give. Other authors have expressed similar views based on pathological findings.

The nearly normal condition of the motor cranial nerves in our case, notwithstanding the existence of symptoms pointing to bulbar involvement, is not difficult to explain. The pyramidal tract was degenerated above the level of these nuclei and consequently the central neurons of the motor cranial nerves were probably affected, causing in this way symptoms of bulbar paralysis. Oppenheim (l. c.) observed symptoms pointing to disease of the ninth, tenth and eleventh nerves in amyotrophic lateral sclerosis, but no changes in the nuclei of these nerves were found. Hoche[43] has been able, in recent hemiplegia and in amyotrophic lateral sclerosis, to trace fibres by the method of Marchi which leave the medial part of the pyramidal tract, pass into the raphe, and cross transversely to the facial nucleus of the opposite side. He has also traced the connection of the hypoglossus nucleus with the pyramidal tract.

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[40] Spiller: The Journal of Nervous and Mental Disease, 1897.

[41] Kronthal: Neurologisches Centralblatt, 1891, p. 133.

[42] Oppenheim: Archiv. für Psychiatrie, xxiv., p. 758.

[43] Hoche: Neurologisches Centralblatt, 1897, p. 245, and Archiv für Psychiatrie, xxviii., p. 980

The fibres of the pyramidal tracts are not entirely destroyed in our case of amyotrophic lateral sclerosis, and the degeneration is less intense than that seen after cerebral lesions. This has been noted by several investigators in other cases of this disease.

Hoche[44] found that the Marchi method did not stain to any extent the pyramidal tracts of the cord, oblongata, and pons in his study of amyotrophic lateral sclerosis, but showed numerous black dots in the crus. The degenerated motor tracts could be traced into the central gyri. This is in favor of the ascending nature of the degeneration, for Marchi's method is only available for recent degeneration, and Hoche's findings are in accordance with the ascending course of the symptoms in many cases. In our case we have sought to find recent degeneration by Marchi's method, but have not been able to employ tissue from a lower level than that of the thalamus. No degeneration of any moment has been detected within the inner capsule, and if a gradually ascending degeneration existed in this case it had not reached the thalamic region.

CONSIDERATIONS ON AMYOTROPHIC LATERAL SCLEROSIS.

By Edward D. Fisher, M.D.

Dr. Fisher considered amyotrophic lateral sclerosis a disease of a character similar to that of progressive muscular atrophy, chronic poliomyelitis, and tabes. All these were simply degenerative diseases of the nervous system. Amyotrophic lateral sclerosis was not an entity, and the name in future would probably be abolished. It was rare, indeed, to find a so-called typical case of progressive muscular atrophy, in which the lesion was confined to the anterior horns. The same might be said of tabes, the lesion extending beyond the posterior columns, involving the lateral tracts, and also the peripheral nervous system. The so-called systemic or tract diseases were relics of an old-time nomenclature, which would ultimately disappear. In all these diseases the physician had to deal with diffuse affections of the spinal cord, medulla and brain. The author presented microscopical sections from a case which, he said, was a typical clinical picture of amyotrophic lateral sclerosis, and which showed disease of both lateral and posterior columns and of the anterior horns.

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[44] Hoche: Neurologisches Centralblatt, 1897, p. 242.

Dr. William C. Krauss, of Buffalo, presented some specimens for microscopic examination which showed the characteristic lesions of amyotrophic lateral sclerosis, together with a slight sclerosis of the posterior columns, more particularly of the columns of Goll. He stated that the specimens had been handed to him for examination and he did not know much about the clinical history of the case.

DISCUSSION.

Dr. Dercum referred to the fact that the case reported by himself and Dr. Spiller was in the beginning apparently one of lateral sclerosis, the lateral column symptoms preceding, without any doubt, the muscular atrophy. When the latter did make its appearance, it did so in the usual manner, affecting first the hypothenar and thenar eminences. The bulbar symptoms were probably referable to changes in the cerebral motor tracts above the nuclei of the medulla oblongata.

Previous to his death the man had lost at various times control over the bladder and rectum, and at such times catheterization was necessary; the lesion of the bladder found at the necropsy may have had its origin in this fact. Nevertheless, the lesion certainly indicated an impaired resistance of the tissues of the bladder, and in this sense was trophic.

Dr. Dercum said he was not prepared to go as far as Dr. Fisher in regarding tabes as being actually related to the disease which we know as amyotrophic lateral sclerosis.

Dr. Charles K. Mills, of Philadelphia, thought that the microscopical studies in a case like the one reported in the paper of Drs. Dercum and Spiller were of great practical value to the clinician. It is only by work of this character that we shall succeed in placing upon a firm foundation the various types of these degenerative nerve diseases, interpret their phenomena, and study them from a more comprehensive standpoint. The literature quoted by Dr. Dercum and Dr. Spiller showed how frequently different portions of the nervous system—different systems of neurons—are attacked in these diseases; it also showed how one is attacked with less intensity than another.

Dr. Mills did not believe that a disease existed which could be properly classed as primary lateral sclerosis. The case reported by Drs. Dercum and Spiller fortified this view, and it was further strengthened by another case of his own which he had not yet reported, but which he had had an opportunity to study for many years and finally to examine on the postmortem table. When this patient had first come under his observation at the University Hospital it was a question whether the case was one of hysteria of the spastic type, or of primary lateral sclerosis. He remained under more or less constant observation for several years, and during this period the symptoms of so-called primary lateral sclerosis gradually developed, with contractures, and, later, bulbar symptoms.

Dr. Mills expressed the opinion that there are three distinct types, or rather sub-types, of this disease. In one type the symptoms of so-called primary lateral sclerosis develop early and contractures and bulbar symptoms later; in the second type muscular atrophy in the limbs is contemporaneous with the beginning of the spastic condition, and in the third type special bulbar symptoms develop very early.

He was in accord with the remark made by Dr. Fisher that amyotrophic lateral sclerosis should be removed entirely from the classification of spinal diseases. It cannot be regarded as purely cerebral, or spinal, or peripheral, but should be recognized as an affection of a special systems of neurons which have been attacked by a degenerative process, perhaps due to a virus, which may possess an elective affinity for certain neurons.

Dr. P. C. Knapp, of Boston, believed that many neurologists were in accord with Dr. Fisher in his rejection of amyotrophic lateral sclerosis as a pathological entity. The present situation in regard to the classification of these diseases is somewhat analogous to that of the muscular dystrophies. A few years ago several clinical types of the latter were described with great accuracy, according to the groups of muscles affected, and now we have merged those clinical types into one disease.

Dr. Knapp said that while the three types of typical amyotrophic lateral sclerosis, progressive spinal muscular atrophy beginning in the thumb muscles, and typical bulbar paralysis, mentioned by Dr. Mills were well recognized, many transitional types were met with which did not absolutely fit any one of them. We must recognize that there is but one pathological entity in the whole process.

The speaker questioned Dr. Fisher's statement regarding the frequency of syphilis as an etiological factor in these cases. It was certainly much less common in cases of degeneration of the motor region of the central nervous system than of the sensory region, namely, in tabes.

Dr. H. M. Thomas, of Baltimore, said he agreed with Dr. Knapp that no satisfactory distinction could be drawn between the three types of progressive muscular atrophy—amyotrophic lateral sclerosis, progressive muscular atrophy (type Aran-Duchenne) and progressive bulbar paralysis. For the proper understanding of the question we must take into consideration the historical development of this disease. When Charcot described amyotrophic lateral sclerosis all forms of progressive muscular wasting were included in the title, "progressive muscular atrophy," and were believed to be due to a primary disease of the ventral horns. This included what we now call the muscular dystrophies as well as some other diseases. From this great group Charcot distinguished certain cases which had a sharp, clinical picture. The disease began with a spastic paralysis of the arms, and this was followed by a diffuse wasting of the paralyzed muscles. Spastic rigidity of the legs was associated with this, and later the bulbar muscles were involved. The anatomical picture corresponding to this was a lesion in the pyramidal tracts combined with one of the ventral horns. The lesion in the pyramidal tracts, Charcot believed to be primary. To this disease he gave the name amyotrophic lateral sclerosis. About the same time, Leyden described the same anatomical findings in cases of progressive bulbar paralysis. In these cases the spastic condition of the limbs had not been present during life. Leyden thought that the disease might be primarily anywhere in the motor path. After attention had been called to this sclerosis of the pyramidal tracts, it was found more and more frequently; so much so that some authors, Gowers among them, believed that it was a constant lesion and that there were no cases in which the disease was confined to the ventral horns, the lesion which Charcot had considered characteristic of the Aran-

Duchenne type of progressive muscular atrophy. Later observations have shown that certain rare cases occur in which the disease is confined entirely to the lower motor segment. It is, however, impossible to distinguish these cases clinically. The muscular spasm, upon which Charcot laid such stress, occurs, as he described it, in only a few of the cases in which the characteristic lesions of amyotrophic lateral sclerosis are found after death. It may vary in every degree, even to complete flaccidity with loss of the deep reflexes. If the term, amyotrophic lateral sclerosis, is used in its purely anatomical sense, or if it is used to characterize those cases which follow the clinical picture which Charcot drew, it may, perhaps, be allowable, but it cannot be used, as is the custom, in both these senses. The name itself is a bad one, combining as it does a symptom —muscular atrophy—and a disease process of the central nervous system—lateral sclerosis—which are really not dependent upon each other. It seemed to Dr. Thomas better not to use the name and to class these three diseases under the general title of progressive (central) muscular atrophy, for it is probable that they all are simply variations of one and the same disease which sometimes begins in the upper motor segment, sometimes in the lower, and usually involves both. Bulbar paralysis would represent the group in which the motor nuclei in the medulla oblongata are involved early or extensively.

Dr. Spiller, in closing, said he felt perfectly sure that disease of the anterior horns could exist without degeneration of the pyramidal tracts. He stated, in regard to the relation of tabes to amyotrophic lateral sclerosis, that a man might have degeneration of the lateral columns and later a similar affection of the posterior columns; indeed, one process might possibly predispose to the other, but it could not be said that the two diseases were related. Dr. Spiller said that we have no satisfactory evidence that amyotrophic lateral sclerosis is due to a virus.

Dr. Fisher, in closing, said the discussion on the two papers had clearly shown just what the present opinion of neurologists is regarding this class of affections. Eventually, he thought, the influence of the past would be shaken off, and a new and more correct classification of these diseases would result. The pure types of this class of affections, which were formerly described, are as a matter of fact rarely met with; there are many transitional types, but no distinct clinical entities.